Defining Treatment Resistance in DBS for Depression
A Systematic Review and Meta-Analysis
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Background
Major depressive disorder (MDD) is a common psychiatric condition with a prevalence of 8.9 million medication-treated adults in the United States, approximately 31% being treatment-resistant depression (TRD). There is a wide selection of treatment options for treatment resistant depression (TRD) including antidepressant combinations, atypical antipsychotics, inflammatory-immune based, psychotherapy, and neuromodulatory. Of the neuromodulatory options, deep brain stimulation (DBS) is one of the most invasive, costly, and low-volume treatments being trialed for TRD.

Prior literature has found only 19% of investigational studies for antidepressant therapies utilized commonly described criteria for treatment resistance including two prior treatment failures with adequate dose confirmation and 4 weeks duration or longer. We sought to characterize the role of DBS in TRD through identification of treatment resistance and efficacy analysis in published randomized controlled trials.

Methods
- Searched Pubmed, Embase, and Cochrane Library through December 2023 via PRISMA guidelines with MeSH terms “deep brain stimulation”, “DBS”, “depression”, “treatment resistant depression” and “TRD”.
- Included randomized controlled trials with reporting of either Hamilton depression rating scale (HDRS) or Montgomery–Asberg depression rating scale (MADRS).
- Reported patient clinical characteristics were collected and graded through the Thase and Rush Model.
- Meta-analysis of DBS efficacy was completed via Revman using random effects and standardized mean differences.

Results
- Thirteen articles met inclusion criteria with 260 patients total.
- Lifetime depressive episodes ranged from an average of 4.7 (5) to 51.2 (76.1).
- Mean lifetime trials of antidepressant medications ranged from 7.9 (3.6) to 22.8 (2.6).
- Four studies required an adequate trial of psychotherapy.
- One reported therapy hours.
- 90% of the total patients (227/251) had a history of ECT.
- Prior ECT procedures per patient ranged from 13.3 to 68.9 (103.6).
- DBS showed efficacy in reducing HDRS/MADRS scores over sham stimulation (SMD -0.49, -1.11 to 0.14, 95% CI p = 0.13).

Conclusion
Interstudy variability in inclusion criteria, definitions of adequate trials and reporting of clinical treatment history made uniform assessment of treatment resistance difficult between studies. Most patients had various trials of antidepressant medication and some form of ECT (unilateral/bilateral) prior to DBS.

Stimulation resulted in reduction of depression scores, however, was not statistically significant. Future randomized controlled trials for treatment resistant disease should rigidly define inclusion criteria.

References